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EXAMINER

ANGELL, JON E

ART UNIT PAPER NUMBER

1635

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/868,732

Applicant(s)

ANDERSSON ET AL.

Examiner

Jon Eric Angell

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 and 24-38 is/are pending in the application.
- 4a) Of the above claim(s) 10-17 and 24-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 36-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>8/2001</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Action is in response to the communication filed on 5/5/04. The amendment has been entered. Claims 1-17 and 24-38 are currently pending in the application and are addressed herein.

Election/Restrictions

Applicant's election without traverse of Group I (1-9 and 36-38) in the reply filed on 2/23/04 is acknowledged. It is noted that new claims 28-38 have been added. Newly submitted claims 28-35 are directed to an invention that is independent or distinct from the elected invention. Claims 28-35 are drawn to an isolated nucleic acid and therefore belong to Group II as indicated in the previous Office Action (restriction requirement). It is noted that the restriction requirement for Group II including reasons for restriction, was set forth in the previous Office Action.

Claims 10-17 and 24-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/23/04.

Claims 1-9 and 36-38 are examined herein.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 8/2/01 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification/Sequence Rules

The specification is objected to for the following reasons:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 because (for example) paragraphs 53, 54 and 69 comprise disclosure of nucleotide sequences which require sequence identifiers (SEQ ID NO), but no SEQ ID NO has been assigned to the sequences. It is noted that the Paper sequence listing discloses several oligonucleotide sequences (see SEQ ID NOS: 1-9). It appears that the improper sequences (e.g., see paragraphs 53, 54 and 69) merely need to be assigned the appropriate SEQ ID NOS., as indicated in the Paper sequence listing. However, should new SEQ ID NOS need to be assigned, a new paper listing and CRF would need to be submitted.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 4, 7 and 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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The instant claims are drawn to method for selecting an animal for having desired genotypic properties comprising testing said animal for the presence of a parentally imprinted quantitative trait locus (QTL) wherein the animal “comprises a pig” (claims 3, 4, and 7) or where the animal “comprises a breeding animal or an animal destined for slaughter” (claims 37 and 38). It is unclear how animal can comprise a pig, a breeding animal or an animal destined for slaughter as “comprising” is open language. For instance, as written the claims encompass an animal that comprises a pig (or a breeding animal or an animal destined for slaughter) as well as other animals. It is unclear how an animal can comprise a pig (or any animal) and also comprise another animal. Claims 1 and 36 are claims from which claims 3, 4, 7, 37 and 38 depend, therefore claims 1 and 36 must broadly encompass all limitations of the dependent claims. Therefore the instant claims are indefinite.

It is noted that amending the claims to indicate that the animal “is a pig” “is a breeding animal” or “is an animal destined for slaughter” would obviate this rejection.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

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relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a method for selecting an animal having desired genotypic properties wherein the method comprises testing the animal for the presence of a parentally imprinted quantitative trait locus (QTL), and includes (1) selecting pigs wherein the QTL maps to about position 2p1.7, (2) the QTL being related to the muscle mass and/or fat deposit of the animal, (3) the QTL comprising at least a part of an IGF-2 gene, (4) the QTL comprising a marker characterized as nt241(G-A) or as Swc9, (5) the paternal or maternal allele of the QTL being predominantly expressed in the animal, (6) testing a nucleic acid comprising a fragment of a QTL, and (7) the animal comprises a breeding animal or animal destined for slaughter.

Therefore, the broadest claims encompass a method of testing any animal for the presence of a parentally imprinted QTL (or a fragment of the QTL) wherein the QTL can be associated with any desired genetic property. As such, the claims encompass a method for identifying a genus of QTLs wherein each species of the genus can have a different structure and different function. For instance, the QTLs encompassed by the claims include QTLs which comprise different nucleotide sequences (e.g., different polymorphisms, alleles of different genes) which can be associated with different phenotypes (e.g., muscle mass, fat deposit or any other desired phenotypic trait). Therefore, the claims encompass a genus of indeterminate size, but which could easily encompass millions of different QTLs, including QTLs which are structurally and functionally unrelated and QTLs which have yet to be identified.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a parentally imprinted QTL whose presence can be used to identify an animal having a desired genotypic property. The specification does not identify any particular sequence structure or particular function must be conserved, nor is there any disclosure of QTL functional fragments. Furthermore, the prior art only appears to disclose one particular parentally imprinted QTL, which is a QTL associated with growth and fat deposit in pigs (e.g., see Andersson 1994 and Andersson-Eklund 1998, both cited by Applicants, see IDS). Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of

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the invention and reference to a potential method of isolating it. The compound itself is required.

See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai*

Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only parentally imprinted QTL associated with a desired genotypic property is the QTL comprising the IGF-2 gene and a marker characterized as nt241(G-A) or as Swc9, wherein the QTL is associated with fat deposit in pigs. There is insufficient written description of the genus of QTLs encompassed by the claims.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-9 and 36-38 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for identifying a porcine having a paternally imprinted QTL wherein the method comprises identifying the presence of the IGF-2 gene having the nt241(G-A) polymorphism in the genome of said porcine using the [the specific oligonucleotides used to identify the QTL in the working example* (e.g., the IGF-2nt245(G-A) specific primer and the SWC9 primer)] wherein said IGF-2 gene co-localizes with the SWC9 microsatellite marker and wherein the presence of said QTL is correlated with decreased fat deposit in said porcine.

*it is noted that the specification is not currently in compliance with the sequence rules. Inserting the appropriate SEQ ID Nos is required.

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Does not reasonably provide enablement for the full breadth of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

The nature of the invention

The instant claims are drawn to method for selecting an animal for having desired genotypic properties comprising testing said animal for the presence of a parentally imprinted quantitative trait locus (QTL). Therefore, the nature of the invention is a method of identifying an animal which has a desired genetic trait wherein the animal can be used to produce offspring that have the desired phenotypic trait.

The breadth of the claims

The claims are very broad and encompass identifying an animal having any parentally imprinted QTL wherein the QTL can be associated with any desired genotypic property and wherein the QTL is correlated to a phenotypic effect in any type of animal, including animals of different species. Additionally, the claims encompass a functional fragment of a QTL. As

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indicated above the claims encompass a genus of QTLs that includes possibly millions of different QTLs including QTLs that have unrelated structures and functions.

The unpredictability of the art and the state of the prior art

With respect to the genus of parentally imprinted QTLs, it appears that the only parentally imprinted QTL disclosed in the prior art is the QTL described by Andersson (1994, see IDS) and Andersson-Eklund (1998, see IDS). Both Andersson and Andersson-Eklund teach a method wherein a QTL of chromosome 4 was shown to be a parentally imprinted QTL correlated to fat deposits in pigs (e.g., see Andersson: page 17, Table 3; and Andersson-Eklund: page 697, Table 3 and page 699, first column 3rd full paragraph). It is noted that the QTL taught by Andersson-Eklund is most likely the same QTL identified by Andersson, as acknowledged by Andersson-Eklund (see page 699: first column, 3rd full paragraph). Andersson and Andersson-Eklund teach a QTL that appears to be a paternally imprinted QTL correlated to back fat depth (e.g., see Table 3 in both references).

The prior art does not appear to disclose any other parentally imprinted QTLs.

Furthermore, the prior art teaches that identification of a QTL associated with a particular phenotype in one species of animal is not indicative that the QTL will be correlated to the same phenotype in all species. For instance, **Pandya et al. (American Journal of Human Genetics 1994)** teaches that although IGF-1 and IGF-2 (as well as their respective receptors) have been associated with body size in mice, there is “no evidence that the IGF-1 locus is imprinted in man”. Therefore, the prior art teaches that the identification of a correlation of a phenotype and

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a QTL in one species does not indicate that there is a correlation between the phenotype and QTL in all species of animals.

The prior art also indicates that a single amino acid substitution in a polypeptide can greatly alter the function of the polypeptide. Specifically, **Witkowski et al. (Biochem. 1999, 38:11643-11650)** teaches that a single amino acid substitution of an active site cysteine with glutamine changes a beta-ketoacyl synthase to a malonyl decarboxylase (e.g., see abstract, and Table 1 on page 11647). Therefore the prior art teaches that genetic alterations, even at the single amino acid level can change the function of a molecule. Therefore, the only specific polymorphism of the IGF-2 gene which can be correlated to fat deposit is the specific nt241(G-A) polymorphism of the porcine IGF-2 gene.

Working Examples and Guidance in the Specification

The specification has identified one specific paternally imprinted QTL which is correlated to decreased fat deposit in pigs, that QTL being the QTL comprising the porcine IGF-2 gene having the nt245(G-A) polymorphism wherein the QTL co-localizes with the SWC9 microsatellite marker. Therefore, the only method of identifying an animal having a desired genotypic property that is disclosed by the specification is a method for selecting a porcine having a paternally imprinted QTL wherein the QTL comprises the IGF-2 gene having the nt241(G-A) polymorphism and which co-localizes with the SWC9 microsatellite marker, wherein the presence of the QTL is correlated with decreased fat deposit in pigs.

Quantity of Experimentation

Considering the vast number of QTLs encompassed by the claims, an enormous amount of additional experimentation would be required in order for one of skill in the art to be able to

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make and use the full scope of the claimed invention. For instance, one would have to identify parentally imprinted QTLs having a correlation to a desired genotypic property. Considering every possible QTL and desired genotypic property encompassed by the claims, this would be a daunting effort.

The art also teaches that although a genetic element (i.e. QTL) may be associated with a particular effect in one species of animal, does not necessarily indicate the same genetic element will be associated with the same effect in all species of animals. Also, the art indicates that a single genetic alteration in a gene can alter the function of that gene. Therefore, additional experimentation would have to be done in order to overcome these art-recognized problems.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the nature of the invention, the breadth of the claims, the unpredictable nature of the invention as recognized in the prior art, the limited amount of working examples and guidance provided, and the high degree of skill required to practice the invention, it is concluded that the specification does not provide an enabling disclosure for the full scope of instant claims. Therefore, additional experimentation is required before one of skill in the art could make and use the claimed invention. The amount of additional experimentation required to perform the broadly claimed invention is undue.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 8 and 36-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Andersson et al. (Science 1994, cited in IDS).

The instant claims are drawn to a method for selecting an animal having desired genotypic properties wherein the method comprises testing the animal for the presence of a parentally imprinted quantitative trait locus (claim 1, 36), wherein the method further comprises testing for the presence of a QTL (claim 2), wherein the QTL is related to potential muscle mass and/or fat deposit (claim 5, 38), wherein the paternal allele of the QTL is predominantly expressed in the animal (claim 8), wherein the animal comprises a breeding animal or animal destined for slaughter (claim 37).

Andersson teaches the making of a quantitative trait loci (QTL) correlated to growth and fatness in pigs wherein the QTL is present on porcine chromosome 4 (e.g., see abstract, Table 3). It is noted that Andersson identified the QTL by crossing (mating) a male wild boar with a female domesticated Large White pig. The wild boars, in general, grow slower, have shorter small intestines, and have more fat deposits than the domesticated Large White pigs. Analyzing the heterozygous F2 generation offspring from the wild boar X Larger White pig crossing, it was determined that the heterozygous F2 offspring comprised a higher “average back fat depth” than the pure-bred Large White pigs. Furthermore, it was determined that this trait (i.e. average back

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fat depth) was not merely an additive effect of each chromosome, but that the trait exhibited a dominance effect (e.g., see Table 3). Furthermore, Andersson teaches,

“The gene action at those loci on chromosome 4 and 13 which were significant at the 5% level appeared to be largely additive, that is, the phenotypic value of the heterozygotes was intermediate to the two homozygotes, except that there was an indication of dominance for increased fat depth (Table 3).” (See p.1772, second to last paragraph).

Therefore, Andersson clearly teaches that the “average back fat depth” (BF) trait is an imprinted QTL that is present on chromosome 4. It is noted that the BF trait is a trait that was passed from the sire (i.e. the male wild boar) to the F2 offspring and exhibit dominance over the sow’s allele in those heterozygous F2 pigs. This clearly indicates that the QTL is a paternally imprinted QTL as the phenotypic effect of the sire's allele was dominant over the effect the sow's allele. As such, Andersson clearly anticipates the instant claims.

Claims 1, 2, 5, 8 and 36-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Andersson-Eklund et al. (J. Animal Sci., 1998, cited in IDS).

The instant claims are drawn to a method for selecting an animal having desired genotypic properties wherein the method comprises testing the animal for the presence of a parentally imprinted quantitative trait locus (claim 1, 36), wherein the method further comprises testing for the presence of a QTL (claim 2), wherein the QTL is related to potential muscle mass and/or fat deposit (claim 5, 38), wherein the paternal allele of the QTL is predominantly expressed in the animal (claim 8), wherein the animal comprises a breeding animal or animal destined for slaughter (claim 37).

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Andersson-Eklund also teaches a paternally imprinted QTL correlated to back fat depth in pigs wherein the QTL is present on chromosome 4 (e.g., see Table 3). It is noted that Andersson-Eklund teaches that this is most likely the same QTL as that taught by Andersson. Specifically, Andersson-Eklund teaches,

“This QTL, located on chromosome 4, is most likely identical to the previously reported QTL for abdominal fat and back fat depth (Andersson et al. 1994) which has been confirmed in subsequent generations (Marklund et al. unpublished data). This was the only QTL found at which there was an indication of dominance effects. The result agrees well with Andersson et al. (1994), who reported that there was an indication of dominance for increased backfat depth on chromosome 4.” (See p.699, first column, second to last paragraph).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell
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DAVE TRONG NGUYEN
PRIMARY EXAMINER